Published by Oxford University Press on behalf of the International Epidemiological Association
International Journal of Epidemiology 2008;37:353–355
doi:10.1093/ije/dym203

Letter to the Editor

Male circumcision and the risk of HIV infection in men who have sex with men

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The suggestion by two decades of observational epidemiological data[1,2] of a partially protective effect of male circumcision on HIV acquisition in heterosexual men has now been confirmed in three randomized controlled trials conducted in sub-Saharan Africa.[3–5] Together these trials show that male circumcision reduces the incidence of HIV infection in sexually active, heterosexual men by at least half. However, we are not aware of a published systematic synthesis of the available evidence on the effect of male circumcision on the risk of HIV infection in men who have sex with men. We thus undertook a systematic review to describe the association between male circumcision and HIV acquisition in men who have sex with men.

We systematically searched Medline and Embase for studies published between 1980 and December 2006 which assessed the effect of male circumcision on HIV infection among men who have sex with men. We combined terms related to men who have sex with men (e.g. men who have sex with men, gay, homosexual), male circumcision (e.g. circumcision, foreskin removal) and HIV infection (e.g. HIV, AIDS) and supplemented the search with references from selected articles, abstracts from the International AIDS Conferences up to 2006 and correspondence with other researchers. Two authors (SLF and CSW) independently assessed the identified studies and selected those which enrolled men who have sex with men who were HIV negative at baseline and which reported risk estimates or number of HIV infections by circumcision status. For each study, data on study methods, participants, interventions (method of establishing circumcision status i.e. self-report, partner-report or by direct observation) and outcome (number HIV infected) were extracted.

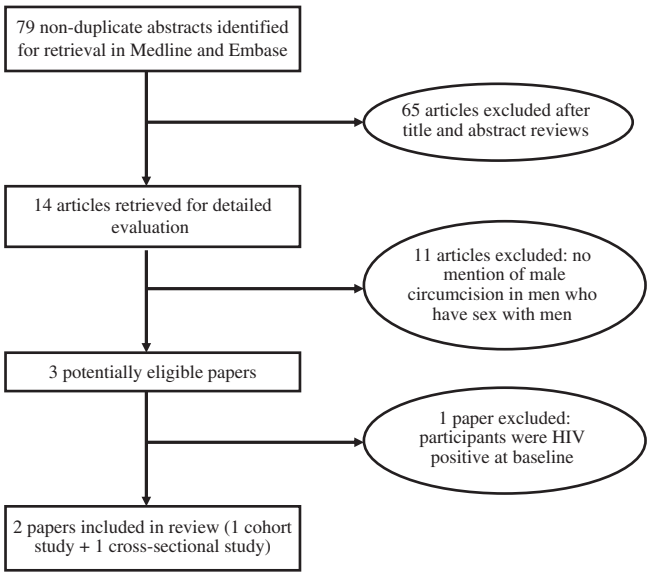

Figure 1 Flowchart of the study selection process

We resolved disagreement between the authors on study eligibility and extracted data by consensus. We used The Cochrane Collaboration's Review Manager to analyse the data.

We summarize the search and selection of studies in Figure 1, the characteristics of included studies in Table 1 and the effect estimates (odds ratios, OR) with 95% confidence intervals (CI) in Figure 2. Of 79 non-duplicate studies identified, 14 were retrieved for detailed evaluation. The list of studies is available from the authors, on request. Two studies, one cohort[6] and one cross-sectional,[7] met our inclusion criteria. A third study that examined the relationship between circumcision status in men who have sex with men, depending on whether they practised unprotected insertive or receptive anal intercourse, was excluded because at baseline all the participants were HIV infected.[8] The cohort study, a prospective study of 3257 HIV-negative men in six cities in the United States,[6] found the incidence of HIV to be lower in circumcised men compared to their uncircumcised counterparts (OR 0.52, 95% CI 0.29–0.93, $P = 0.03$). The cross-sectional study of 499 men in Seattle[7] found a lower HIV prevalence among circumcised than in uncircumcised men (OR 0.46, 95% CI 0.26–0.81, $P = 0.009$). In each study,

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SL Fankem and CS Wiysonge contributed equally to this work and share joint first authorship. CA Hankins is guarantor of the article.

Table 1 Characteristics of included studies

Study	**Buchbinder[6]**
Methods	Prospective cohort study of men who have sex with men, from the HIV Network for Prevention Trials (HIVNET), conducted in six US cities: Boston, Chicago, Denver, New York, San Francisco and Seattle. This study was conducted between April 1995 and May 1997. All local institutional review boards approved the study protocol and written informed consent was obtained from all participants. Study participants were seen every 6 months over an 18 month period for HIV pre-test counselling, testing and behavioural interviews. HIV post-test counselling occurred at separate visits 2 weeks later.
Participants	Participants were HIV negative men at study enrollment and reported having anal sex (protected or not) with a man in the previous 12 months. They were recruited from prior cohort studies, sexually transmitted disease clinics, bars and dance clubs, advertising, street outreach and referral from other participants. 3257 men enrolled into the study; 87.7% were circumcised.
Interventions	Circumcision was assessed by self-report.
Outcomes	HIV status established by antibody test (tests not specified).
Study	**Kreiss[7]**
Methods	Cross-sectional study of men who have sex with men conducted in Seattle, Washington, USA. This study was conducted between April 1989 and March 1991 from two clinics that provide comprehensive health care to HIV-infected patients and from the AIDS Prevention Project which conducts an HIV screening and counselling program. Men, 17–64 years old, reporting a history of homosexual behaviour were invited to participate.
Participants	Men reporting a history of homosexual behaviour and attending any of two AIDS clinics or the AIDS Prevention Project were included. 503 men enrolled into the study, (316 HIV-seropositive and 186 seronegative). Final analysis included 499 men (97%) of which 85% were circumcised.
Interventions	Circumcision was assessed by self-report.
Outcomes	HIV status established by ELISA test and confirmed by Western Blot or immunofluorescent assays.

circumcision status was assessed by self-report. There was no distinction in either study between the frequencies of insertive vs receptive anal sex by circumcision status. Despite the differences in study methodology, the findings were consistent between the two studies (pooled OR 0.49, 95% CI 0.32–0.73, $P = 0.0006$; heterogeneity $P = 0.79$, $I^2 = 0$).

The observational nature of the studies included in this systematic review raises the possibility that the observed effect might be due to confounding factors not measured (and therefore not controlled for) in the studies, rather than being the result of a biological effect of male circumcision. In addition, ascertainment bias can be a problem in any study of male circumcision based on self-report because in some settings self-report has been found to have poor sensitivity and specificity for ascertaining real circumcision status.[9]

Studies of men who have sex with men have identified unprotected receptive anal intercourse as a practice with the greatest risk of HIV infection,[10] suggesting that the circumcision status of the insertive partner may be an important variable influencing risk for receptive partners. Thus, there is need for randomized controlled trials to find out if circumcised men who have sex with men are both at lower risk of HIV acquisition themselves and, if infected, less likely to transmit HIV than uncircumcised men who have sex with men. However, it should be clearly stated that the benefits of male circumcision could be undermined by increases in unsafe sexual behaviour (such as non-use of condoms and multiple concurrent sex partners) sparked by decreases in perceived risk.[11]

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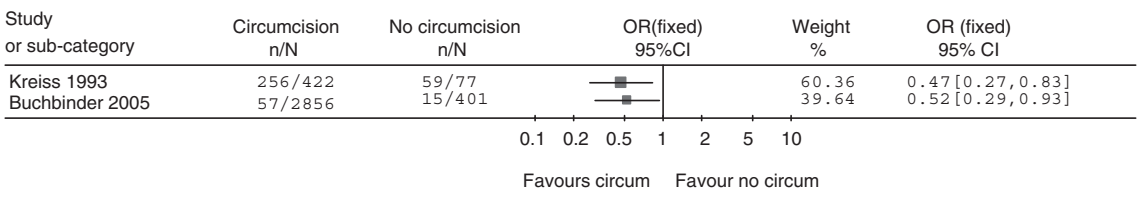

Figure 2 Effect of male circumcision on HIV acquisition in men who have sex with men (circum: circumcision)

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